

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 2

Amendments to the Claims

This listing of claims will replace all prior versions and listings of the claims in the application.

Claims 1-118 (Cancelled).

--119. (Currently amended) A composition which comprises:

- a) a conjugate ~~comprising of~~ (i) a GM2 ganglioside derivative which comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;
- b) QS-21, a saponin derivable from the bark of a Quillaja saponaria Molina tree; and
- c) a pharmaceutically acceptable carrier;

wherein the amount of the conjugated GM2 ganglioside derivative is an amount between about 1 μ g and about 200 μ g, the amount of the saponin is an amount between about 10 μ g and about 200 μ g, and the GM2:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2,

wherein in the conjugate the ganglioside derivative is covalently bound to the Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin. --

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 3

Claims 120-125 (Cancelled).

--126. (Currently amended) The composition of claim ~~[[125]]~~ 119 wherein the amount of the saponin is about 100 µg. --

--127. (Currently amended) The composition of claim ~~[[125]]~~ 119 wherein the amount of the saponin is about 200 µg.--

Claim 128 (Cancelled).

--129. (Currently amended) The ~~[[A]]~~ composition of claim 119 which comprises:

- a) a conjugate ~~comprising of~~ (i) a GM2 ganglioside derivative which comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;
- b) QS-21, a saponin derivable from the bark of a Quillaja saponaria Molina tree, ~~wherein the saponin is QS-21~~; and
- c) a pharmaceutically acceptable carrier;

wherein the conjugated GM2 ganglioside derivative is present in an amount between about ~~10 µg and about 50 µg~~ 1 µg and about 200 µg, the amount of the saponin is about 100 µg and the GM2:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, where the amount of such conjugate and such saponin is effective to stimulate or enhance production in a subject of an antibody to GM2;

and wherein in the conjugate the ganglioside derivative is covalently bound to the Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ε-aminolysyl group of Keyhole Limpet Hemocyanin. --

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 4

--130. (Previously presented) A method of treating a subject afflicted with melanoma which comprises administering to said subject an amount of the composition of claim 129 effective to stimulate or enhance production in a subject of an antibody to GM2 and to thereby treat said melanoma in said subject. --

--131. (Currently amended) A method of stimulating or enhancing production of an antibody directed to GM2 in a subject which comprises administering to the subject an effective amount of a composition which comprises:

- a) a conjugate ~~comprising of~~ (i) a GM2 ganglioside derivative which comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;
- b) QS-21, a saponin derivable from the bark of a Quillaja saponaria Molina tree; and
- c) a pharmaceutically acceptable carrier;

wherein the amount of the conjugated GM2 ganglioside derivative is an amount between about 1 μ g and about 200 μ g, the amount of the saponin is an amount between about 10 μ g and about 200 μ g, and the GM2:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody directed to GM2,

wherein in the conjugate the ganglioside derivative is covalently bound to the Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin so as to thereby stimulate or enhance production in said subject of the antibody directed to GM2. --

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 5

--132. (Currently amended) A method of treating a human subject having cancer ~~cancer in a subject~~ which comprises administering to the subject an effective ~~cancer treating~~ amount of a composition which comprises:

- a) a conjugate ~~comprising~~ of (i) a GM2 ganglioside derivative which comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;
- b) QS-21, a saponin derivable from the bark of a Quillaja saponaria Molina tree; and
- c) a pharmaceutically acceptable carrier;

wherein the amount of the conjugated GM2 ganglioside derivative is an amount between about 1 μ g and about 200 μ g, the amount of the saponin is an amount between about 10 μ g and about 200 μ g, and the GM2:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2,

wherein in the conjugate the ganglioside derivative is covalently bound to the Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin so as to stimulate or enhance production in the subject of the antibody to GM2 and thereby treat the ~~cancer in the~~ subject.

--133. (Previously presented) The method of claim 132, wherein the cancer is of epithelial origin. --

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 6

--134. (Previously presented) The method of claim 132, wherein the cancer is of neuroectodermal origin. --

--135. (Previously presented) The method of claim 134, wherein the cancer of neuroectodermal origin is a melanoma.--

--136. (Previously presented) The method of claim 131 or 132, wherein the administering is effected at two or more sites. --

--137. (Previously presented) The method of claim 136, wherein the administering is effected at three sites. --

--138. (Previously presented) The method of claim 131 or 132, wherein the composition is administered subcutaneously to said subject.--

--139. (Previously presented) The method of claim 138, wherein the composition is administered to said subject at two-week intervals.--

--140. (Previously presented) The method of claim 138, wherein the composition is initially administered to said subject at weekly intervals. --

--141. (Previously presented) The method of claim 131 or 132, wherein the composition to be administered is prepared prior to administration to the subject by mixing the conjugate and the saponin.--

--142. (Previously presented) The method of claim 141, wherein the conjugate and the saponin are mixed on the day of administration to the subject. -

Claim 143 (Cancelled).